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Particle modelling using advanced image analysis and deep learning

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In recent decades, processes including particles like fermentation, flocculation, precipitation and crystallization have become essential parts of various bioprocesses. In many of these processes, particle properties are direct or indirect measures of product quality and process efficiency (Redman & O'Grady, 2017). With the currently increasing demand for optimizing these processes and ensuring more consistent product properties, there has been a renewed focus on continuous particle analysis, which previously has been too time consuming task. Recent advances in advanced image analysis have now opened up for directly measuring and analysing particles in real time.

In this work, a generic real-time monitoring and modelling framework for particle processes is presented, based on population balance modelling, utilizing deep-learning techniques for rate-estimations. Using a novel flow-cell microscopy setup, captured microscopy images are continuously provided as inputs to the neural network alongside the controlled process variables including temperature and pH at the current and a given future time. The neural network will here estimate the rates for particle birth, growth and death, and provide forecasts of the particle size/shape distributions at the future time, by solving a generic population balance model. The training of the neural network model can be carried out in real-time, whilst the given process is running, continuously improving the process model, and hence the generated process forecast.

The framework is demonstrated through an industrial scale pharmaceutical crystallization case study. Here it is shown that by using the raw images as an input to the neural network, it is possible to effectively pick up visually detectable disturbances, which can then be taken into account in the model predictions, improving the model predictions significantly in comparison to only using the controlled process variables as inputs.

Redman, T., & O'Grady, D. (2017). "Improve products and processes with inline particle analysis." CHEMICAL ENGINEERING PROGRESS, **113**(8): 47-55.